D. Remarks/Argument

Reconsideration of this application is respectfully requested. Upon entry of the amendments, claims 1-6 and 9-15 will be pending. Claims 7 and 16-17 are canceled herein without prejudice or disclaimer to being pursued in a later filed application. Applicants address the Examiner's comments below.

Priority

The priority application on which the instant application is based was filed on March 19, 2003. A certified copy of this translated priority document is concurrently submitted herewith and made of record in accordance with the provisions of 37 C.F.R. § 1.55. Applicants respectfully request that the instant application be given the priority date of March 19, 2003.

Sequence Compliance

The Specification has been objected to for failing to comply with the requirements of 37 CFR § 1.821-1.825. Specifically, Figures 1 and 7B do not describe the required sequence identifier in either the drawings or the Brief Description of the Drawings section of the application.

Applicants have herein amended the specification to include the appropriate sequence identifier in the Brief Description of the Drawings section of the application and provided a substitute Sequence Listing incorporating SEQ ID NO:11. The Specification has also been

amended to incorporate the substitute sequence listing. These changes are believed to overcome the objections. Reconsideration and withdrawal are respectfully requested.

Enablement

The Examiner rejects claims 4, 6, 10, 11, 14, and 15 for lack of enablement under 35 USC § 112, ¶ 1. According to the Examiner, while the claims are enabling for use of the invention *in vitro*, the claims do not reasonably provide enablement for the full scope of a pharmaceutical composition that requires a treatment effect *in vivo*. Based on the application of the *Wands* factors (breadth of the claims, unpredictability of the art, amount of direction, existence of working Examples, etc.), the Examiner concludes that undue, *de novo* experimentation would have been required by one of ordinary skill in the art at the time of filing to make and use the claimed invention over its entire scope. Applicants respectfully disagree.

Although the instant specification does not contain *in vivo* data regarding use of the antisense oligonucleotides for inhibiting HIV, Examples 4 and 5 of the instant specification confirm that antisense oligonucleotides of the claimed invention inhibit HIV-1 activity in cells transfected with the virus. Furthermore, Applicants assert that one of skill in the art at the time of invention would have accepted the disclosed model as reasonably correlating to the condition of HIV and as reasonably predictive of the use of the antisense oligonucleotide in humans for treating same. In contrast to the Examiner's assertion (*see* Office Action at page 7), a rigorous or an invariable exact correlation is not required. *See also* MPEP § 2164.02. Nor is a correlation of efficacy between animal subjects the standard for determining enablement as the Examiner seems to suggest. *See* Office Action at pages 7-9. Such a standard would necessarily require

that Applicants submit data from human clinical trials overseen by the FDA. However, it is improper for the Patent Office to request evidence regarding the degree of effectiveness of a compound in humans.

Moreover, as of the filing date of the instant application, the state of the art was such that specific animal models existed for testing new drugs to treat HIV and such models were available to those of ordinary skill in the art. For example, the SCID-hu mouse model of HIV infection (developed by SyStemix in the early 1990's) was widely known and readily available for use by those of ordinary skill in the art as of the filing date for preclinical evaluation of anti-HIV compounds such as those of the claimed invention. Thus, contrary to the portrayal of the status of the art as given by the articles cited by the Examiner, evaluation of the antiviral effect of a particular composition *in vivo* involved no more than routine experimentation and not undue trial and error experimentation as suggested by the Examiner.

Here, the consideration of the *Wands* factors and the evidence as a whole favor enablement of the claimed invention. A plain reading of the instant specification shows that it contains detailed disclosure on:

1. how to make the antisense oligonucleotides of the invention (*see, e.g.*, Example 1);
2. how to use the antisense oligonucleotides for anti-HIV therapy (*see, e.g.*, paragraphs [0051] through [0055] of the published application); and
3. that the oligonucleotides, in fact, exhibit anti-HIV activity activity against the virus (*see* Examples 4 and 5).

Accordingly, Applicants submit that one skilled in the art at the time of invention would have been able to make and use the claimed invention, over the full scope of the claims as amended, without undue experimentation.

Notwithstanding the above, and without acceding to the propriety of the Examiner's argument and rejection, Applicants have herein amended claims 4, 6, 10, 11, 14, and 15 to recite compositions comprising the oligonucleotides of the invention and a pharmaceutically acceptable carrier or diluent, as suggested by the Examiner. Applicants believe that these amended claims encompass any composition (pharmaceutical or otherwise) that comprises the antisense oligonucleotides as disclosed by the instant application. The amendment is believed to overcome the rejection. Reconsideration and withdrawal are respectfully requested.

Novelty

Claims 1 and 2 (and 5 and 12) are rejected as anticipated by U.S. Patent No. 5,847,096 to Schubert et al. ("Schubert"). Specifically, the Examiner contends that SEQ ID NO:33 disclosed in Schubert meets the limitations of claims 1 and 2 (and 5 and 12). Applicants traverse as the rejection may apply to the claims as amended.

Claims 1 and 2 (from which claims 5 and 12 directly depend) have been amended herewith to clarify that the oligonucleotide consisting of at least 15 successive nucleotides complementary to the nucleotide residues of 6-44 of SEQ ID NO:1 is an antisense oligonucleotide.

SEQ ID NO:33 as disclosed in Schubert, and as depicted by the alignment provided by the Examiner, is a sense oligonucleotide. Accordingly, the teachings of Schubert do not meet each and every limitation of claims 1 and 2 (and 5 and 12). Thus, the rejection should be withdrawn.

Obviousness

Claims 5 and 12 are alternatively rejected as obvious in view of Schubert under 35 U.S.C. § 103(a). According to the Examiner, SEQ ID NO:33 disclosed by Schubert meets the structural limitations of claims 5 and 12 and can therefore be considered an anti-HIV agent capable of hybridizing to SEQ ID NO:1 as recited by the claims. Applicants traverse as the rejection may be applied to the claims as amended.

Claims 1 and 2 have been amended herein as indicated above. Claims 5 and 12 are dependent from claims 1 and 2, respectively, and thereby incorporate all of the limitations of the claim. Schubert does not teach or suggest the antisense oligonucleotides encompassed by claims 1 and 2, nor anti-HIV agents incorporating same. Accordingly, Applicants believe the amendment overcomes the rejection. Reconsideration and withdrawal is requested.

Claims 1-6 and 9-15 are rejected as obvious over U.S. Publication No. 2005/0222068 to Mourich et al. ("Mourich") in view of Galderisi et al. ("Galderisi"). According to the Examiner, one of skill in the art would have been motivated to use the phosphorothioate internucleotide bonds taught by Galderisi in combination with SEQ ID NO:18 disclosed by Mourich, which is an antisense oligonucleotide that is complementary to 15 successive nucleotides of SEQ ID NO:1 and that inhibits viral replication of HIV in cells, to achieve the claimed invention. Applicants traverse.

Without addressing the merits of the rejection, Applicants note that Mourich was filed on October 21, 2004 claiming priority to an application filed October 23, 2003. The

application published on October 6, 2005. In contrast, the instant application claims priority to a Japanese application filed on March 19, 2003, a certified copy of which has been provided herewith. Accordingly, Applicants assert that Mourich is not available as prior art, and that, consequently, the combination of Mourich and Galderisi as a basis to reject the claims cannot stand. Reconsideration and withdrawal of the obviousness rejection is requested.

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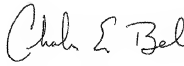
Applicants submit that this paper is fully responsive and that the application is in condition for allowance. Such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

With a one-month petition for extension of time and payment of the corresponding fee, this response is due on or before February 4, 2008 (the nominal due date of February 3, 2008 occurring on a Sunday). The Commissioner is hereby authorized to charge payment of any additional fees that may be required, or credit any overpayment of same, to Deposit Account No. 08-1935, Reference No. 2352.008.

Respectfully submitted,



Dated: February 4, 2008

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